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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,516	01/16/2002	Xianqiang Li	26757-710	1568

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EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 11/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,516	LI ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The applicant's response filed 8/13/2004 has been entered. Claims 1-17 are pending.

1. Claims 1-17 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kain et al. (6,306,600, issued October 23, 2001) in view of Anderson et al. (6,548,249, issued April 15, 2003).

Kain et al. disclose a fusion protein comprising green fluorescent protein (GFP) as a reporter and short live protein, mouse ornithine decarboxylase (See column 2, lines 30-33) for studying protein degradation (See column 2, lines 13-18). The EGFP-MODC fusion protein can be used in drug screening. GFP fluorescence can be detected intracellularly without performing any additional steps (See column 4, lines 25-28). The invention is a method of assaying activation or deactivation of promoters or other transcriptional or translational elements with a transient fluorescent reporter protein, comprising the steps of transfecting cells with an expression vector comprising a fusion protein (See column 7, lines 66-67 and column 8, lines 1-11). The differences of the fluorescence intensity between cells expressing the fluorescent protein under different transcriptional or translational elements of interesting is rapidly detected. Further, the transfected cells are treated with a compound of interest to determine the effect of the compound of interest on the transcriptional or translational elements. A change in fluorescence upon treatment of the cells with the compound of interest is also rapidly detected (See column 8, lines 11-22). The invention is also used to study cell lineage (See column 8, lines 24-25). The transfected cells as well as cycloheximide treated cells were analyzed for fluorescence intensity by FACS (See column 9, lines 19-35). It is suggested that a population of cells can be selected by different reporter signal intensities. The half-life of the fusion protein

was determined by blocking protein synthesis with cycloheximide (See column 10, lines 32-35). The transfected cell line can be used for much analysis, for example, drug that inhibits protein degradation after the addition of cycloheximide (See column 13, lines 60-67). It is suggested that the drug is an agent, which affects the degradation rate of the protein.

Kain et al. do not disclose expressing a different fusion protein in each cell and under different growth conditions and that the selected population of cells contacted with a plurality of agents, which may affect protein degradation rates.

Anderson et al. disclose the invention related to the use of scaffold proteins, green fluorescent protein in fusion constructs with random and defined peptides and peptides libraries (See the Abstract). Each random peptide in the library is different (See column 2, lines 17-29). One of the random peptides is ornithine decarboxylase (See column 21, lines 10-13), which is short-lived fusion protein. The condition for fusion protein expression will vary with the choice of the expression vector and the host cell and will be easily ascertained by one skilled in the art through routine experimentation (See column 42, lines 40-44). It suggested that the cells expressing fusion protein will be grow under different growth conditions based upon the needs. The invention comprises introducing a molecular library of fusion nucleic acids encoding randomized peptides fused to scaffold into a plurality of cells. Each of the nucleic acids comprises a different nucleotide sequences encoding scaffold with a random peptide. The plurality of cells is then screened (See column 45, lines 64-67 and column 46, lines 1-5). The cells are isolated by FACS (See column 47, lines 50-55). A cell with an altered phenotype is detected, and the presence of fusion protein is verified to ensure that the peptide was expressed (See column 47, lines 41-44). It is suggested that each cell has a different fusion protein. The

screening methods of the invention may be useful to screen a large number of cell types under a wide variety of conditions (See column 49, lines 20-29).

One of ordinary skill in the art would have been motivated to modify the method of Kain et al. by expressing a different fusion protein in each cell within a library of cells, and contacting the selected population of cells with a plurality of agents which may affect protein degradation rates and under different growth condition as taught by Anderson et al.. The motivation is that the method of Anderson et al. allows the creation of a peptide library that is easily monitored, both for its presence within cells and its quantity and the peptides within or fused to a scaffold are being accessible for interaction with potential functional targets (See column 4, lines 52-56) and the screening methods of the invention may be useful to screen a large number of cell types under a wide variety of conditions (See column 49, lines 20-29). It would have been prima facie obvious to modify the method of Kain et al. by expressing a different fusion protein in each cell within a library of cells, and contacting the selected population of cells with a plurality of agents which may affect protein degradation rates and under different growth condition for screening the agents that affect protein degradation rates, monitoring the expression of short-live proteins under different growth conditions and screening the differences in short lived proteins expressed by first and second cell sample.

The response argues that Kain et al. teaches a method of inhibiting further expression of a single fusion protein, e.g. EGFP-MODC in cell and Anderson et al. fail to teach or suggest the claimed methods of utilizing cells expressing a library of different fusion proteins to screen for agents that are contacted with the cells and affect degradation of the different fusion proteins.

The response next argues that Kain et al. focus on the studies of degradation of a single fusion protein and does not give a clue as to whether or why a library of different fusion proteins should be expressed and agents should be screened for their effects on degradation of the fusion protein after the agents are contacted with the cells expressing the fusion proteins.

However, Kain et al. disclose the degradation of expressed protein was detectable by adding cycloheximide to block protein synthesis and the cell lines can be used to screen for drugs that inhibit protein degradation after the addition of cycloheximide (See column 13, lines 57-67). Anderson et al. disclose constructing fusion protein with random and defined peptides and peptides libraries (See the Abstract). Each random peptide in the library is different (See column 2, lines 17-29). Anderson et al. also disclose that the plurality of cells is then screened for a cell exhibiting an altered phenotype and the altered phenotype is due to the presence of a bioactive peptide (See column 46, lines 1-5). Anderson et al. disclose the list of way to alter the phenotype of the cells (See column 46, lines 6-34). Thus, the teachings of Anderson et al. suggest that the agent(s)/condition(s) affecting degradation of the fusion protein is the one way to alter the phenotype of the cells. Therefore, one of ordinary skill in the art would have been motivated to modify the method of Kain et al. by applying the teachings of Anderson et al. as discussed above to make the instant invention. The motivation is that the method of Anderson et al. allows the creation of a peptide library that is easily monitored, both for its presence within cells and its quantity and the peptides within or fused to a scaffold are being accessible for interaction with potential functional targets (See column 4, lines 52-56) and the screening methods of the invention may be useful to screen a large number of cell types under a wide variety of conditions (See column 49, lines 20-29). It would have been prima facie obvious to modify the method of

Kain et al. by applying the teachings of Anderson et al. for making the instant invention. The rejection is maintained.

Summary

2. No claims are allowable.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

5. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung J.T
October 28, 2004

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
10/28/04